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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,604	01/31/2002	Michael Alan Reeve	PA-9912	8189

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PATENT DEPARTMENT
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EXAMINER	
CHUNDURU, SURYAPRABHA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,604	REEVE ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,14-18,21-25 and 27-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,14-18,21-25 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on November 5, 2003 has been entered.

2. Claims 1-2, 4-11, 14-18, 21-25, 27-30 are pending Claims 3, 12, 13, 19-20, 26,are cancelled.

3. This application filed on January 31, 2002 is a 371 of PCT/GB00/00916 filed on March 10, 2000, which claims foreign priority to EP 99301933.0 filed on March 12, 1999.

Response to Arguments

4. Applicant's response to the office action (Paper No.8) is fully considered and is found persuasive in part.

5. With regard to the objections made in the previous office action regarding sequence non-compliance, IDS, Fig.1, use of trademark, and preferred layout of the specification, claims, Applicants arguments and amendment are fully considered and the objections are withdrawn herein in view of the arguments and amendments.

6. With regard to the rejection made in the previous office action under 35 USC 112, second paragraph with reference to the terms 'affected DNA and unaffected DNA', Applicants' arguments are fully considered and found not persuasive. Applicants' argue that the terms are defined in the instant specification (page 2, lines 5-17). As stated in the MPEP 2145, "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims". In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993), the instant claims do not recite this limitation and specification can not be read into the claims. Therefore the rejection is maintained herein.

7. With regard to the rejections made in the previous office action under 35 USC 112 second paragraph, with reference to claim 15 (mathematical notation (n!) and (n-r)!) and claim 29, Applicants' arguments are fully considered and the rejections are withdrawn herein in view of the arguments.

8. With regard to the rejection made in the previous office action under 35 USC 102(e) as anticipated by Wagner, Applicants arguments have been fully considered and found persuasive in part. Applicants argue that Wagner does not teach methodology for obtaining mixtures of DNA fragments enriched in fragments are characteristic of a phenotype. This argument is found not persuasive because on column 31, lines 6-21, Wagner clearly indicates mixing of wild-type (unaffected) and mutant (affected) DNA fragments and capturing hetero-duplex (which contain mutations) or hybrids using immobilized MBP. Thus MBP is used in isolating hetroduplexes formed. The instant claims are in comprising format and does not exclude any additional step to recover the hybrids that contain mutations, which is also supported by the instant claim 6, which recites this additional step of using a mismatch-binding protein. Thus claim 1 and 6 are clearly anticipated by Wagner. With regard to phenotype characterization, Wagner disclose on columns 35-36, 63, 64, identification of a specific allele (mutation) which confers resistance to Scrapie, a prion disease related to Creutzfeld-Jacob disease in humans. The dependent claim 5, is anticipated by Wagner, because Wagner teaches affected DNA (mutation containing DNA) from cells of an individual that show the phenotype (resistance to scarpie) and unaffected DNA (wild-type) is DNA from the individual the do not show the phenotype of interest (see column 35, lines 62-67, column 36, lines 1-62, column 63, lines 31-35, column 64, lines 1-2); claims 7-8 are anticipated by Wagner, because Wagner discloses the wild-type and mutant DNA fragments are

tagged by one member of a specific binding pair (biotin-labeled oligonucleotide) (see column 31, lines 6-21); Claim 10 is anticipated by Wagner because Wagner discloses mixing hybrids with excess of test DNA (mutant or affected DNA) to form duplexes and enrichment of perfectly matched duplexes (see column 36, lines 46-62, column 63, lines 31-35, column 63, lines 1-17); Claim 11 is anticipated by Wagner, because the affected and the unaffected DNA is fragmented with restriction endonuclease enzymes (which include four and six-cutter enzymes) (see column 40, lines 1-21).Thus the rejection is maintained for the claims 1, 5-8, 10-11 and the rejection is withdrawn with regard to claims 2, 4, 9, 14-16, 23-25, and 29.

9. With regard to the rejections made in the previous office action under 35 USC 102(e) as anticipated by Dong et al., Applicants arguments have been fully considered and rejections are moot in view of the arguments and new grounds of rejection.

10. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants arguments have been fully considered and rejection is moot in view of the arguments and new grounds of rejection.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Gifford (USPN. 5,750,335).

Gifford teaches a method of claim 1, 29, of providing a mixture of DNA fragments enriched in fragments that are characteristic of a phenotype of interest, wherein, Gifford discloses that the method comprises

(a) mixing the fragments of the affected DNA (test or mutant) and the fragments of the unaffected DNA (standard or reference) fragments under hybridizing conditions to form hybrids (see column 3, lines 41-50, column 4, lines 10-17);

(b) recovering a mixture of hybrids that contain mismatches (see column 3, lines 50-55);

(c) recovering fragments of the affected DNA from the mixture of hybrids that contain mismatches (see column 3, lines 50-55, column 4, lines 56-65, column 5, lines 37-66); with regard to DNA fragments characterized of a phenotype, Gifford teaches that a patient having genetic defect is taken as test or affected DNA and the corresponding normal gene sequence having normal gene function is taken as unaffected DNA (see column 11, lines 60-67).

With regard to claims 2-5, Gifford also teaches that the affected DNA is pooled DNA of one or more individuals that show the phenotype of interest and the unaffected DNA is pooled DNA of one or more individuals who do not show the phenotype (see column 4, lines 25-40, column 8, lines 33-47, column 9, lines 45-48);

With regard to claim 6, Gifford teaches that the recovery of hybrids is performed using a mismatch-binding protein (MBP) (see column 3, lines 50-55, column 4. lines 12-23);

With regard to claims 7-8, Gifford teaches that the affected or unaffected DNA fragments are tagged with appropriate labels like radioactive labels, chromogenic or chemiluminscent labels such as biotin (see column 10, lines 33-49);

With regard to claim 9, Gifford teaches that the heteroduplex hybrids having characteristic phenotype are self-hybridized to form duplexes and subsequently perfect matched duplexes are recovered (see column 13, lines 59-64, column 11, lines 7-19, column 19, lines 1-13);

With regard to claim 11, Gifford teaches fragmentation of affected and unaffected DNA using restriction endonuclease enzymes (see column 9, lines 66-67, column 11, lines 60-63);

With reference to claim 14, Gifford teaches a method of making a set of arrays of fragments of interest (see column 9, lines 60-67, column 10, lines 1-30, column 18, lines 40-55) wherein the method comprises (a and B) fragmenting genomic DNA (see column 9, lines 57-67); (c) ligating adapters (PCR tails) to the digested fragments (see column 10, lines 1-4); (d-e) selectively amplifying tailed fragments using PCR primers that are complementary to the tail sequences (see column 10, lines 4-7); (f) forming an array of the tailed fragments (representative fragments); (g) and repeating the steps using one or more differrent subsets of restriction endonucleases (see column 10, lines 10-11);

With regard to claim 15, Gifford teaches repeating the steps with different multiple restriction endonucleases result in differential tail ligation and yield different array of fragments (see column 10, lines 20-26);

With regard to claim 16, Gifford teaches that restriction endonucleases include 4-6 cutter enzymes (see column 24, lines 15-34);

With regard to claims 17-18, Gifford teaches M13mp8 which comprises n restriction endonucleases (n includes 3-10) and 3 restriction endonucleases are selected to fragment the DNA (see column 24, lines 15-34);

With regard to claims 23-25, Gifford teaches that the method of claim 14 further comprises observing a pattern of hybridization using a set of arrays (representational difference analysis, column 22, lines 29-56, Fig. 8);

With regard to claims 27-28, Gifford also teach obtaining a double stranded DNA molecule obtainable by cutting the DNA molecule by means of one or more restriction enzymes, having different length from other fragment; resolvable by electrophoresis from one another and mapping the locations of differences in DNA molecules (see column 22, lines 32-46);

With regard to claim 30, Gifford teaches one of the primers is tagged or labeled (see column 18, lines 31-39). Thus the disclosure of Gifford meets the limitations in the instant claims.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782 . The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
March 11, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/16/04